Dkt. 70442-PCT-US/JPW/BJA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Eric Kandel, et al.
U.S. Serial No.	:	10/582,303
Filed	:	as §371 national stage of PCT/US2004/041388, filed December 9, 2004
For	:	GRP RECEPTOR-RELATED METHODS FOR TREATING AND PREVENTING FEAR-RELATED DISORDERS

1185 Avenue of the Americas
New York, New York 10036
July 18, 2007

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following items numbered 1-61 which are also listed on the accompanying substitute Form PTO-1449, attached hereto as **Exhibit A**. Items 1-9 are either U.S. patents or U.S. patent application publications. Pursuant to 37 C.F.R. 1.98(a)(2)(ii), no copies of references 1-9 are being included herewith. Copies of items 10-61 are attached hereto as **Exhibits 1-52**, respectively. Applicants request that the Examiner review the items listed and make them of record in the subject application.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3), before the issuance of a first Office Action on the merits. Accordingly, no fee is required.

1. U.S. Patent No. 4,870,009, issued to Evans et al. on September 26, 1989;

2. U.S. Patent No. 6,552,061, issued to Kitazawa et al. on April 22, 2003;

3. U.S. Patent No. 5,741,651 issued to Feldman et al. on April 21, 1998;

4. U.S. Patent No. 5,814,463, issued to Spindel et al. on September 29, 1998;

5. U.S. Patent No. 6,817,756, issued to Lee et al. on February 13, 2001;

6. U.S. Patent No. 6,200,546, issued to Hoffman et al. on March 13, 2001;

7. U.S. Patent No. 5,620,955, issued to Knight et al. on April 15, 1997;

8. U.S. Patent No. 6,307,017, issued to Coy et al. on October 23, 2001;

9. U.S. Patent No. 6,566,080, issued to Kopin et al. on May 20, 2003;

10. Bachevalier, J. et al. (2001). Effects of selective neonatal temporal lobe lesions on socioemotional behavior in infant rhesus monkeys (*Macaca mulatta*). Behav. Neurosci. 115(3), 545-559 **(Exhibit 1)**;

11. Baron-Cohen, S. et al. (2000). The amygdala theory of autism. Neurosci. Biobehav. Rev. 24(3), 355-364 **(Exhibit 2)**;

12. Bast, T. et al. (2001). The ventral hippocampus and fear conditioning in rats. Different anterograde amnesias of fear

after tetrodotoxin inactivation and infusion of the GABA(A) agonist muscimol. Exp. Brain Res. 139(1), 39-52 **(Exhibit 3)**;

13. Belmont, L.D., and Mitchison, T.J. (1996). Identification of a protein that interacts with tubulin dimers and increases the catastrophe rate of microtubules. Cell 84(4), 623-631 **(Exhibit 4)**;

14. Bolshakov, V.Y. et al. (1997). Recruitment of new sites of synaptic transmission during the cAMP-dependent late phase of LTP at CA3-CA1 synapses in the hippocampus. Neuron 19(3), 635-651 **(Exhibit 5)**;

15. Bolshakov, V.Y. et al. (2000). Dual MAP kinase pathways mediate opposing forms of long-term plasticity at CA3-CA1 synapses. Nat. Neurosci. 3(11),1107-1112 **(Exhibit 6)**;

16. Bourtchouladze, R. et al. (1998). Different training procedures recruit either one or two critical periods for contextual memory consolidation, each of which requires protein synthesis and PKA. Learn. Mem. 5(4), 365-374 **(Exhibit 7)**;

17. Brauer, A.U. et al. (2001). Perforant path lesion induces up-regulation of stathmin messenger RNA, but not SCG10 messenger RNA, in the adult rat hippocampus. Neuroscience 102(3), 515-526 **(Exhibit 8)**;

18. Cook, E.H. et al. (1998). Linkage-disequilibrium mapping of autistic disorder, with 15q11-13 markers. Am. J. Hum. Genet. 62(5),1077-1083 **(Exhibit 9)**;

19. Davis, M., and Whalen, PJ. (2001). The amygdala: vigilance and

emotion. Mol. Psychiatry 6(1), 13-34 **(Exhibit 10)**;

20. Dulac, C., and Axel, R. (1995). A novel family of genes encoding putative pheromone receptors in mammals. Cell 83(2), 195-206 **(Exhibit 11)**;

21. Fanselow, M.S., and LeDoux, J.E. (1999). Why we think plasticity underlying Pavlovian fear conditioning occurs in the basolateral amygdala. Neuron 23(2), 229-232 **(Exhibit 12)**;

22. Frederickson, C.J. et al. (2000). Importance of zinc in the central nervous system: the zinc-containing neuron. J. Nutr. 130, 1471S-1483S **(Exhibit 13)**;

23. Goddard, A.W. et al. (2001). Reductions in occipital cortex GABA levels in panic disorder detected with ^{1}H-magnetic resonance spectroscopy. Arch. Gen. Psychiatry 58(6), 556-561 **(Exhibit 14)**;

24. Hampton, L.L. et al. (1998). Loss of bombesin-induced feeding suppression in gastrin-releasing peptide receptor-deficient mice. Proc. Natl. Acad. Sci. USA 95, 3188-3192 **(Exhibit 15)**;

25. Harrel, A.V. et al. (2001). Transgenic mice over-expressing the 5-HT3 receptor have enhanced learning in latent inhibition and contextual fear conditioning paradigms. Soc. Neurosci. Abstr., Program No. 853.11, 31st Annual Meeting, San Diego, California **(Exhibit 16)**;

26. Hellmich, M.R. (1999). Multiple protein kinase pathways are involved in gastrin-releasing peptide receptor-regulated secretion. J. Biol. Chem. 274(34), 23901-23909 **(Exhibit 17)**;

27. Huang, Y.Y., and Kandel, E.R. (1998). Postsynaptic induction and PKA-dependent expression of LTP in the lateral amygdala. Neuron 21(1), 169-178 **(Exhibit 18)**;

28. Hubank, M., and Schatz, D.G. (1994). Identifying differences in mRNA expression by representational difference analysis of cDNA. Nucleic Acids Res. 22(25), 5640-5648 **(Exhibit 19)**;

29. Ishikawa-Brush, Y. et al. (1997). Autism and multiple exostoses associated with an X;8 translocation occurring within the *GRPR* gene and 3' to the *SDC2* gene. Hum. Mol. Genet. 6(8), 1241-1250 **(Exhibit 20)**;

30. Johansson, B. et al. (2001). Hyperalgesia, anxiety, and decreased hypoxic neuroprotection in mice lacking the adenosine A1 receptor. Proc. Natl. Acad. Sci. USA 98(16), 9407-9412 **(Exhibit 21)**;

31. Kapp, B.S. et al. (1992). Amygdaloid contributions to conditioned arousal and sensory information processing. In: The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction, J.P. Aggleton, ed. (New York: Wiley-Liss), pp. 229-254 **(Exhibit 22)**;

32. Krezel, W. et al. (2001). Increased anxiety and synaptic plasticity in estrogen receptor β-deficient mice. Proc. Natl. Acad. Sci. USA 98(21), 12278-12282 **(Exhibit 23)**;

33. Kroog, G.S. et al. (1995). Mammalian bombesin receptors. Med. Res. Rev. 15, 389-417 **(Exhibit 24)**;

34. LeDoux, J.E. (2000). Emotion circuits in the brain. Annu. Rev.

Neurosci. 23, 155-184 **(Exhibit 25)**;

35. Lee, K. et al. (1999). Bombesin-like peptides depolarize rat hippocampal interneurones through interaction with subtype 2 bombesin receptors. J. Physiol. 518(3), 791-802 **(Exhibit 26)**;

36. Low, K. et al. (2000). Molecular and neuronal substrate for the selective attenuation of anxiety. Science 290,131-134 **(Exhibit 27)**;

37. Mahanty, N.K., and Sah, P. (1998). Calcium-permeable AMPA receptors mediate long-term potentiation in interneurons in the amygdala. Nature 394, 683-687 **(Exhibit 28)**;

38. Malleret, G. et al. (1999). 5-HT1B receptor knock-out mice exhibit increased exploratory activity and enhanced spatial memory performance in the Morris water maze. J. Neurosci. 19(14), 6157-6168 **(Exhibit 29)**;

39. McKernan, M.G., and Shinnick-Gallagher, P. (1997). Fear conditioning induces a lasting potentiation of synaptic currents *in vitro*. Nature 390, 607-611 **(Exhibit 30)**;

40. McKernan, R.M. et al. (2000). Sedative but not anxiolytic properties of benzodiazepines are mediated by the GABA(A) receptor alpha(1) subtype. Nat. Neurosci. 3(6), 587-592 **(Exhibit 31)**;

41. Merali, Z. et al. (1998). Aversive and appetitive events evoke the release of corticotropin-releasing hormone and bombesin-like peptides at the central nucleus of the amygdala. J. Neurosci. 18, 4758-4766 **(Exhibit 32)**;

42. Mermelstein, P.G., et al. (2000). Critical dependence of cAMP response element-binding protein phosphorylation on L-type calcium channels supports a selective response to EPSPs in preference to action potentials. J. Neurosci. 20(1), 266-273 **(Exhibit 33)**;

43. Parent, M.B. et al. (2002). Effects of the antidepressant/antipanic drug phenelzine and its putative metabolite phenylethylidenehydrazine on extracellular gamma-aminobutyric acid levels in the striatum. Biochem. Pharmacol. 63, 57-64 **(Exhibit 34)**;

44. Pitkanen, A. et al. (1997). Organization of intra-amygdaloid circuitries in the rat: an emerging framework for understanding functions of the amygdala. Trends Neurosci. 20(11), 517-523 **(Exhibit 35)**;

45. Ramboz, S. et al. (1998). Serotonin receptor 1A knockout: an animal model of anxiety-related disorder. Proc. Natl. Acad. Sci. USA 95(24), 14476-14481 **(Exhibit 36)**;

46. Rammes, G. et al. (2000). Synaptic plasticity in the basolateral amygdala in transgenic mice expressing dominant-negative cAMP response element-binding protein (CREB) in forebrain. Eur. J. Neurosci. 12, 2534-2546 **(Exhibit 37)**;

47. Rogan, M.T. et al. (1997). Fear conditioning induces associative long-term potentiation in the amygdala. Nature 390, 604-607 **(Exhibit 38)**;

48. Romanski, L.M., and LeDoux, J.E. (1992). Equipotentiality of

thalamo-amygdala and thalamo-cortico-amygdala circuits in auditory fear conditioning. J. Neurosci. 12(11), 4501-4509 **(Exhibit 39)**;

49. Schaeren-Wiemers, N., and Gerfin-Moser, A. (1993). A single protocol to detect transcripts of various types and expression levels in neural tissue and cultured cells: in situ hybridization using digoxigenin-labeled cRNA probes. Histochemistry 100, 431-440 **(Exhibit 40)**;

50. Sharif, T.R. et al. (1997). Functional expression of bombesin receptor in most adult and pediatric human glioblastoma cell lines; role in mitogenesis and in stimulating the mitogen-activated protein kinase pathway. Mol. Cell. Endocrinol. 130, 119-130 **(Exhibit 41)**;

51. Steele, P.M., and Mauk, M.D. (1999). Inhibitory control of LTP and LTD: stability of synapse strength. J. Neurophysiol. 81, 1559-1566 **(Exhibit 42)**;

52. Trepel, C., and Racine, R.J. (2000). GABAergic modulation of neocortical long-term potentiation in the freely moving rat. Synapse 35(2), 120-128 **(Exhibit 43)**;

53. Tsvetkov, E. et al. (2002). Fear conditioning occludes LTP-induced presynaptic enhancement of synaptic transmission in the cortical pathway to the lateral amygdala. Neuron 34(2), 289-300 **(Exhibit 44)**;

54. Wada, E. et al. (1997). Generation and characterization of mice lacking gastrin-releasing peptide receptor. Biochem. Biophys. Res. Commun. 239, 28-33 **(Exhibit 45)**;

55. Wang, C. et al. (2001). Role of NMDA, non-NMDA, and GABA receptors in signal propagation in the amygdala formation. J. Neurophysiol. 86, 1422-1429 **(Exhibit 46)**;

56. Weisskopf, M.G., and LeDoux, J.E. (1999). Distinct populations of NMDA receptors at subcortical and cortical inputs to principal cells of the lateral amygdala. J. Neurophysiol. 81, 930-934 **(Exhibit 47)**;

57. Weisskopf, M.G. et al. (1999). L-type voltage-gated calcium channels mediate NMDA-independent associative long-term potentiation at thalamic input synapses to the amygdala. J. Neurosci. 19(23), 10512-10519 **(Exhibit 48)**;

58. Woodson, W. et al. (2000). Afferents from the auditory thalamus synapse on inhibitory interneurons in the lateral nucleus of the amygdala. Synapse 38(2), 124-137 **(Exhibit 49)**;

59. Yu, B., and Shinnick-Gallagher, P. (1997). Dihydropyridine- and neurotoxin-sensitive and -insensitive calcium currents in acutely dissociated neurons of the rat central amygdala. J. Neurophysiol. 77(2), 690-701 **(Exhibit 50)**;

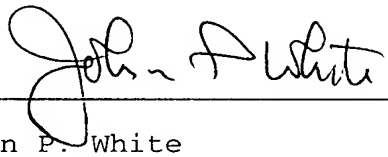
60. International Preliminary Report on Patentability (Chapter I) issued by the International Bureau on behalf of the International Searching Authority on June 12, 2006 in connection with International Application No. PCT/US2004/041388 **(Exhibit 51)**; and

61. PCT/US2004/041388, filed December 9, 2004, published as WO 05/60625 on July 7, 2005 **(Exhibit 52)**.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Supplementary Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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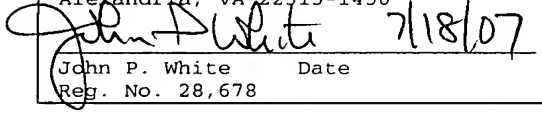

7/18/07

John P. White Date
Reg. No. 28,678

Exhibit A

Form PTO-1449 Substitute	U.S. Department of Commerce Patent and Trademark Office	Application Number	10/582,303
		Filing Date	As §371 national stage of PCT/US04/41388, filed December 9, 2004
		First Named Inventor	Eric Kandel et al.
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Art Unit	
		Examiner Name	
		Attorney Docket No.	70442-PCT-US

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		U.S. 4,870,009	09-26-1989	Evans et al.
		U.S. 6,552,061	04-22-2003	Kitazawa et al.
		U.S. 5,741,651	04-21-1998	Feldman et al.
		U.S. 5,814,463	09-29-1998	Spindel et al.
		U.S. 6,817,756	02-13-2001	Lee et al.
		U.S. 6,200,546	03-13-2001	Hoffman et al.
		U.S. 5,620,955	04-15-1997	Knight et al.
		U.S. 6,307,017	10-23-2003	Coy et al.
		U.S. 6,566,080	05-20-2003	Kopin et al.

FOREIGN PATENT DOCUMENTS

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		WO 05/60625	07-07-2005		

EXAMINER SIGNATURE	DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1]Applicant's unique citation designation number (optional). [2] See Kinds of Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [6] Applicant is to place a check mark here if English Language Translation is attached.

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		Bachevalier, J. et al. (2001). Effects of selective neonatal temporal lobe lesions on socioemotional behavior in infant rhesus monkeys (*Macaca mulatta*). Behav. Neurosci. 115(3), 545-559	
		Baron-Cohen, S. et al. (2000). The amygdala theory of autism. Neurosci. Biobehav. Rev. 24(3), 355-364	
		Bast, T. et al. (2001). The ventral hippocampus and fear conditioning in rats. Different anterograde amnesias of fear after tetrodotoxin inactivation and infusion of the GABA(A) agonist muscimol. Exp. Brain Res. 139(1), 39-52	
		Belmont, L.D., and Mitchison, T.J. (1996). Identification of a protein that interacts with tubulin dimers and increases the catastrophe rate of microtubules. Cell 84(4), 623-631	
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		Cook, E.H. et al. (1998). Linkage-disequilibrium mapping of autistic disorder, with 15q11-13 markers. Am. J. Hum. Genet. 62(5),1077-1083	
		Davis, M., and Whalen, PJ. (2001). The amygdala: vigilance and emotion. Mol. Psychiatry 6(1), 13-34	
		Dulac, C., and Axel, R. (1995). A novel family of genes encoding putative pheromone receptors in mammals. Cell 83(2), 195-206	
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		Frederickson, C.J. et al. (2000). Importance of zinc in the central nervous system: the zinc-containing neuron. J. Nutr. 130, 1471S-1483S	

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		Goddard, A.W. et al. (2001). Reductions in occipital cortex GABA levels in panic disorder detected with ^{1}H-magnetic resonance spectroscopy. Arch. Gen. Psychiatry 58(6), 556-561	
		Hampton, L.L. et al. (1998). Loss of bombesin-induced feeding suppression in gastrin-releasing peptide receptor-deficient mice. Proc. Natl. Acad. Sci. USA 95, 3188-3192	
		Harrel, A.V. et al. (2001). Transgenic mice over-expressing the 5-HT3 receptor have enhanced learning in latent inhibition and contextual fear conditioning paradigms. Soc. Neurosci. Abstr., Program No. 853.11, 31st Annual Meeting, San Diego, California	
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		Hubank, M., and Schatz, D.G. (1994). Identifying differences in mRNA expression by representational difference analysis of cDNA. Nucleic Acids Res. 22(25), 5640-5648	
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		Krezel, W. et al. (2001). Increased anxiety and synaptic plasticity in estrogen receptor β-deficient mice. Proc. Natl. Acad. Sci. USA 98(21), 12278-12282	
		Kroog, G.S. et al. (1995). Mammalian bombesin receptors. Med. Res. Rev. 15, 389-417	
		LeDoux, J.E. (2000). Emotion circuits in the brain. Annu. Rev. Neurosci. 23, 155-184	
		Lee, K. et al. (1999). Bombesin-like peptides depolarize rat hippocampal interneurones through interaction with subtype 2 bombesin receptors. J. Physiol. 518(3), 791-802	

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		Parent, M.B. et al. (2002). Effects of the antidepressant/antipanic drug phenelzine and its putative metabolite phenylethylidenehydrazine on extracellular gamma-aminobutyric acid levels in the striatum. Biochem. Pharmacol. 63, 57-64	
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		Rammes, G. et al. (2000). Synaptic plasticity in the basolateral amygdala in transgenic mice expressing dominant-negative cAMP response element-binding protein (CREB) in forebrain. Eur. J. Neurosci. 12, 2534-2546	
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Form PTO-1449 Substitute	U.S. Department of Commerce Patent and Trademark Office	Application Number	10/582,303
		Filing Date	As §371 national stage of PCT/US04/41388, filed December 9, 2004
		First Named Inventor	Eric Kandel et al.
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)		Art Unit	
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		Attorney Docket No.	70442-PCT-US

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		International Preliminary Report on Patentability (Chapter I) issued by the International Bureau on behalf of the International Searching Authority on June 12, 2006 in connection with International Application No. PCT/US2004/041388	

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